

# COVID-19 Current Drugs with Potential for Treatment: A Review

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## Abstract

The world has experienced major deadly pandemic which proved brutal killer of various intensities such as Antonine flue in 168 AD, than Black Fever, Cholera Asian/Russian flue, HIV/AIDS. Now recently in Dec. 2019 a novel coronavirus called as Severe Acute Respiratory Syndrome Coronavirus (SARS-COV-2) emerged in the Wuhan City of China, and rapidly spreaded worldwide, and on March 11, 2020, World Health Organisation (WHO) declared COVID-19 a world pandemic. As no vaccine or drug is available to eradicate the virus, and as such researchers and scientist of different countries are in the race of preparation of vaccine to eradicate this pandemic and experimenting with drugs and therapies to help ease the strain on hospitals and intensive care units. Some drugs that are indicated for other afflictions seems to be potentially beneficial to treat the infection albeit without unequivocal evidences. Thus the present article is compiled with the objective to review the published literature on the effectiveness of these drugs against COVID-19 which is need of hour.

**Keywords:** Pandemic, Covid -19, Vaccine, Drugs, World Health Organisation, SARS-COV2.

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## INTRODUCTION

The COVID-19 disease caused by the novel Coronavirus belongs to coronavirus family now called as Severe Acute Respiratory Syndrome coronavirus-2 (SARAS COV-2 formerly called 2019-n Cov). Which was first identified amid an outbreak of respiratory illness cases in Wuhan City of China [1]. It was initially reported to the world Health Organisation (WHO) in Dec 31, 2019 and on January 30, 2020 WHO declared the COVID-19 outbreak a global health emergency [2] and finally on March 11 2020, WHO declared COVID-19 a global pandemic, since after declaring H1N1 influenza a pandemic in 2009 [3]. At present i.e. on 11 of Sept. 2020 there are 28.8 million infected persons and 9 lakh 21 thousand deaths worldwide.

Even moderately effective drugs and therapies or their combinations could reduce the crushing demand on hospitals and intensive care units, changing the nature of the risk the new pathogen poses to population and healthcare system. New drugs together with new diagnostic antibody test, patient and contact tracing technologies, disease surveillance and other warning tools, means the anticipated next wave of the global pandemic does not have to be as bad as the first.

It is difficult to carefully evaluate the information emerged during the pandemic to tackle the COVID-19 therapies with in a short time in the early's 2020. Some of the promising drugs /therapies were mentioned below that somehow decline the death rate due to COVID-19 or helps in recovery of patients.

## METHODS

To write up this article, literature search was conducted by using PubMed, Google scholar and science Direct database were selected and searched by searching "COVID-19 treatment, therapies drugs and vaccines". About 57 articles were searched, out of 57 article 47 were found to be relevant related to the topic.

### Some of the Important Drugs/Therapies are as Under Naitazoxanide

(NT-300;; Romark laboratories):- This drug inhibit replication of broad range of respiratory viruses in cell culture including SARS-COV-2. The trails are being held in high risk populations including elderly and healthcare workers. Third pases of clinical trails is palnnd [4].

**Ivermectin**

This is an antiparasitic drug showed in vitro reduction of viral RNA in Vero hSLAM cells 2 hours postinfection with SARS-COV-2 clinical isolate in Australia [5]. But the authors observed that this preliminary study does not translate to human use and what does is required at this early stage. Data from the pharma kinetic revealed that excessive dosing studies indicate that the SARS-COV-2 inhibitory concentration for ivermectin are not likely attainable in human [6].

**Niclosamide**

It is an antihelminthic agent has a potential to use as an antiviral agent. It decrease the protoged infection and transmission has been developed [7].

**Umifenovir (Arbidol)**

This is an antiviral drug that binds to hemagglutinin protein. It is used in china and Russia to treat influenza. The structural and molecular dynamic study reveals that Vankadari Corroborated that the drug target for umifenovir is the spike glycoproteins of SARS-COV-2 similar to that of H3N2 [8].

In india a phase 3 trail combining 2 antiviral agents, favipravir and umifenovir started in May 2020 [9].

**Emetine hydrochloride (Acer Therapeutics)**

It is an active ingredient of syr of ipecac (given orally to induce emesis). Its clinical trails has been conducted for viral hepatitis and varcella-zoster virus infection. It is also a potent inhibitor of multiple genetically distinct coronaviruses. Experts are planning to evaluate the safety and antiviral activity of emetine with an adoptive design phase 2/3 randomised, blinded, placebocontrolled multicentral trail in high risk symptomatic adults with confirmed COVID-19 not requiring hospitalization [10].

**Stannous Protoporphyrin (SnPP, RBT-9; Renibus Therapeutics)**

This is an antiviral agent in phase 2 trail for treatment of COVID-19 patients who are at high risk of health deterioration because of age or morbidities e.g. Diabetese, Kidney or Cardiovascular disease [11].

**Corticosteroids**

These steroid drugs are used to provide relief for inflamed areas of the body. These drugs decrease swellings, itching, redness and allergic reactions. They are used for the treatment of different diseases such as asthma, allergies or skin problem, arthritis etc.

Corticosteroid are not generally recommended for treatment of viral pneumonia [12]. In UK recovery trail assessed the mortality rate at day 28 in hospitalized patient with COVID-19 who received low dose of dexamathasone 6mg Po or IV daily for 10 days added to usual care. It was observed that in dexamathasone

group the incidence of death was lower than the usual care group among patients receiving invasive mechanical ventilation. But not among those who were not receiving respiratory support at randomization [13].

Early guidelines for management of critically ill adults with COVID-19 specified when to use low dose corticosteroid and when to refrain from using corticosteroids. The recommendation for use depend on the precise clinical situation (e.g refractory shock, mechanically ventilated patient with ARDS).

A study in the Netherland showed a 5 day course of high dose corticosteroids accerlated respiratory recovery, lowered hospital mortality rate and reduced the Likelihood of mechanical ventilation in patients with severe COVID-19 associated cytokine storm syndrome compared with historical control [14].

In a conclusive dexamethasone proves to be promising for the treatment of COVID-19 patients.

**Nitric Oxide**

Previous published data reveals that in 2004, SARS-COV has potential role of inhaled nitric oxide as a supportive measure for treating infection in patients with pulmonary complications. Nitricoxide treatment reversed pulmonary hypertension, improved severe hypoxia, and shortenend the length of ventilator support compared with matched control patients with SARS [15]. A phase 3 study (PULSE-CVD-19-001) for iNO (INO Pulse; Bellerophon Therapeutics) was accepted by FDA in March 2020 to evaluate the efficacy and effectiveness, and safety in COVID-19 patients who require supplemental oxygen before the disease progresses to necessitate mechanical ventilation support[16]. The cost of iNo is reported as exceeding \$100/hour.

**Deupirfenidine (LYT-100, Pure Tech Bio)**

Denterated form of pirfenidone, an approved anti-inflammatory and anti fibrotic drug. It inhibits TGF- beta and TNF-alpha. To evaluate use for serious respiratory complications, including inflammation and fibrosis that occurs due to SARS-COV-2 infection, clinical trails started in July2020 [17].

**Multistem Cell Therapy**

It has a potential to produce therapeutic factors in response to signals of inflammation and tissue damage. The first patient has been enrolled in the phase 2/3 trial Multi stem Administration for COVID-19 induced Acute Respiratory Distress syndrome (MACOVIA) at university Hospital's Cleveland Medical Centre [18].

**Convalescent Plasma**

The Convalescent plasma antibody rich products that are collected from eligible donors, who have recovered from COVID-19. This has not yet been

shown effective in COVID-19. The FDA states that it is important to evaluate its efficacy and safety via clinical trials before administering convalescent plasma to patient with COVID-19.

The use of convalescent plasma has a long history in the treatment of infectious disease mentioned in the journal of Clinical Investigation [19].

A meta analysis of 15 controlled studies showed a significantly lower mortality rate in patient with COVID-19 who received convalescent plasma compared with controlled groups. But the author points out that studies were mostly of low or very low quality with a moderate or high risk of bias[20]. However the convalescent plasma therapy improved survival in many COVID-19 patients.

### Remdesivir

The broad spectrum antiviral agent remdesivir is a nucleotide analog prodrug. On May 1, 2020, the US FDA issued their EUA or remdesivir to allow for the severe COVID-19 (confirmed or suspected) in hospitalized adults and children prior to approval [21].

A new drug application for remdesivir was submitted to the FDA in August 2020. A phase 1 trial of inhaled nebulized remdesivir was initiated in late June 2020 to determine if remdesivir can be used on an outpatient basis and at earlier stages of disease.

The first published report with a group of patient receiving remdesivir compassionate use described clinical improvement in 36 of 53 hospitalised patients (68%) with severe COVID-19. At baseline, 30 patient (57%) were receiving ventilation and 4 (8%) extracorporeal membrane oxygenation (ECMO). Measurement of efficacy requires randomized placebo-controlled trials [22].

It was observed that during compassionate use follow up (median of 18 days) includes the following. Oxygen support class improved in 36 patients (68%), including 17 of 30 patients (57%) receiving mechanical ventilation who were extubated. Twenty five patients (47%) were discharged. Seven patients (13%) died.

The mortality rate was 18% (6 out of 34) among patients receiving invasive ventilation and 5% (1 of 19) among those not receiving invasive ventilation.

More findings from the comparative indicated that 74.4% of remdesivir treated patients recovered by day 14 versus 59% of patients receiving standard of care. The mortality rate in patient treated with remdesivir in the analysis was 7.6% at day 14 compared with 12.5% among patient not taking remdesivir . The analysis also found that 83% of paediatric patient and 92% of pregnant and postpartum women with a broad

spectrum of COVID-19 severity recovered by day 28 [23].

The use of remdesivir in 86 pregnant women, (67 while pregnant and 19 on post partum days 0-3). No new safety signals were observed. The results showed that pregnant women had higher rates of recovery than non pregnant adult treated with compassionate use remdesivir (92%) Vs 62% likely owing to the younger age of pregnant women of median age, 33 years vs 64 years. This data was presented at the virtual COVID-19 conference held in July 10-11, 2020 [24].

The coadministration of remdesivir is not recommended with chloroquine or hydroxychloroquine.

### Hydroxychloroquine /Chloroquine

It is an antimalarial drug and is used against several inflammatory disease including lupus and rheumatoid arthritis. Early reports from China and France suggested that patients with severe symptoms of COVID-19 improved more quickly when given Chloroquine or Hydroxychloroquine. In some cases, combination of azithromycin and hydroxychloroquine give positive results.

These two drugs has been shown to kill the COVID-19 viurs in the laboratory dish. This drugs appears to work through two mechanisms. First, they make it harder for the virus to attach itself to the cell, inhabiting the virus from entering the cell and multiplying within it. Second, if the virus does manage to get inside the cell, the drugs kill it before it can multiply. Whereas Azithromycin is never used for viral infection alone or in combination, can treat COVID-19 viral infection. While recent human studies suggest no benefits and possibly a higher risk of death due to lethal rhythm abnormalities. Regarding the effectiveness of Hydroxychloroquine alone to prevent coronavirus infections, the results of clinical trial just published in the New England Journal of Medicine found that it did not prevent infection, but the study is questionable by some experts [25].

### What treatment is currently available to treat Coronavirus

As such there is no specific antiviral treatment for Covid -19. However certain measures must be taken similar to treatment of any viral infection .These are as under:

- a) Take plenty of rest.
- b) Stay well hydrated.
- c) Take immunity boosters.
- d) To reduce fever and ease aches and pains ,take acetammophen .Be sure to follow direction .If taking any combination of cold or flu medicines,keep track of all the ingredients and the doses.For acetammophen,the total daily doses from all products should not exceed 3,000 mg /day.

### COVID-19 Vaccine status in the world:

After the emergence of coronavirus in Wuhun city of China its genetic sequence was studied and published in Jan 11, 2020. After ward there is research and collaboration among scientist and biopharmaceutical companies for the production of vaccine.

Vaccine is a biotechnological product intended to provide acquired immunity against coronavirus disease 2019 (COVID-19). Till date i.e. 5th of September 2020 there are 231 vaccine candidates in development [26]. In august 24 vaccine candidates were announced or undergoing clinical trails with six beginning phase III and 18 still in phase ist and 2<sup>nd</sup>.

Some of the vaccines candidates who are at II or IIIrd clinical trails are as under.

#### Moderna NIAID, BARDA

The technology used is Lipid nanoparticles dispersion containing mRNA. This vaccine is at clinical trail of phase III.

Sinopharm (Beijing Institute of Biological products, Wuhan institute of Biological products) this is at phase III and the technology involved is inactivated SARS-COV2 (vero cells).

#### Coronavac Sinovac

This is at clinical trail of phase III and technology involved is inactivated SARS-COV-2 AZD1222, University of Oxford, Astrazeneca. This vaccine candidate is at III clinical trail with the technology involvement of modified Chimp adenovirus vector (ChAdOXI).

BNT162a1, b1, b2, c2, Bio NTech, Fosun, Pharma Pfizer. This is at II and III clinical trail and is based on mRNA technology

To date, just one coronavirus vaccine has been approved. Sputnik V formely known as Gam COVID-Vac developed by the Gamaleya Research institute in Moscow (Russia) and was approved by the Ministry of Health of Russian Federation on 11 August 2020. But the experts have raised considerable concern about the vaccine's safety and efficacy as it has not yet entered into the III phase of clinical trail.

### COVID-19 vaccine status in India

There are three COVID-19 vaccine in ist and 2 human clinical trails developed indigenously by Bharat Biotech, in collaboration with the Indian Council of Medical Research (ICMR) and Zydus Cadila Ltd, are currently underway.

Serum Institute of India has entered into agreement with Oxford University and Astra Zenec and

has entered into the 3<sup>rd</sup> clinical trail stage in India. For this purpose Govt of India has provided a special manufacturing priority Lincese on fast track, the trail protocol process to get the trail completed with 58 days. Serum institute will be developing this vaccine for 92 other nations under the agreement and deal with oxford and Astra Zeneca [27].

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